

WHAT IS CLAIMED IS:

1. A nanoparticulate composition comprising:
 - (a) nanoparticulate beclomethasone particles, budesonide particles, or a combination thereof, having an effective average particle size of less than about 150 nm; and
 - (b) tyloxapol as a surface stabilizer adsorbed onto the surface of said beclomethasone and/or budesonide particles,
wherein the nanoparticulate composition is sterile filtered.
2. The composition of claim 1, wherein the beclomethasone particles, budesonide particles, or a combination thereof are present in an amount selected from the group consisting of about 99% to about 1% (w/w), about 90% to about 10% (w/w), about 80% to about 30%, and about 80% to about 40% (w/w), based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.
3. The composition of claim 1, wherein the concentration of tyloxapol is selected from the group consisting of from about 0.01 to about 90%, from about 1 to about 75%, from about 10 to about 60%, and from about 10 to about 30% by weight, based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.
4. The composition of claim 1, wherein the effective average particle size of the beclomethasone particles, budesonide particles, or a combination thereof is less than about 120 nm.
5. The composition of claim 1 wherein the effective average particle size of the beclomethasone particles, budesonide particles, or a combination thereof is less than about 100 nm.

6. The composition of claim 1 wherein the effective average particle size of the beclomethasone particles, budesonide particles, or a combination thereof is less than about 80 nm.

7. The composition of claim 1 wherein the effective average particle size of the beclomethasone particles, budesonide particles, or a combination thereof is less than about 50 nm.

8. The composition of claim 1 further comprising at least one secondary surface stabilizer.

9. The composition of claim 8, wherein the secondary surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hydroxypropyl methylcellulose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, poloxamers, poloxamines, charged phospholipids, dioctylsulfosuccinate, Tetronic 1508®, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfates, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isonylphenoxy poly-(glycidol), C₁₈H₃₇CH₂(CON(CH₃)-CH₂(CHOH)₄(CH₂OH)₂, decanoyl-N-methylglucamide, n-decyl β-D-glucopyranoside, n-decyl β-D-maltopyranoside, n-dodecyl β-D-glucopyranoside, n-dodecyl β-D-maltoside, heptanoyl-N-methylglucamide, n-heptyl-β-D-glucopyranoside, n-heptyl β-D-thioglucoside, n-hexyl β-D-glucopyranoside,

nonanoyl-N-methylglucamide, n-noyl β -D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl- β -D-glucopyranoside, octyl β -D-thioglucopyranoside, and random copolymers of vinyl acetate and vinyl pyrrolidone.

10. The composition of claim 8, wherein the secondary surface stabilizer is selected from the group consisting of dioctylsulfosuccinate, sodium lauryl sulfate, hydroxypropylmethyl cellulose, benzalkonium chloride, and polyvinylpyrrolidine.

11. The composition of claim 1, wherein the beclomethasone and/or budesonide particles are crystalline, semi-crystalline, amorphous, semi-amorphous, or a mixture thereof.

12. The composition of claim 1, further comprising one or more pharmaceutically acceptable excipients.

13. The composition of claim 1, wherein the beclomethasone is beclomethasone dipropionate.

14. The composition of claim 1 formulated into an aerosol for nasal or pulmonary administration.

15. A method of making a nanoparticulate composition comprising:
(a) dispersing particles of budesonide, beclomethasone, or a mixture thereof in a liquid dispersion medium; and
(b) applying mechanical means in the presence of grinding media to reduce the average particle size of budesonide, beclomethasone, or a mixture thereof in the liquid dispersion medium to less than about 150 nm, and
(c) sterile filtering the resulting nanoparticulate dispersion;
wherein tyloxapol is added to the liquid dispersion medium before or after milling.

16. The method of claim 15, wherein the beclomethasone particles, budesonide particles, or a combination thereof are present in an amount selected from the group consisting of about 99% to about 1% (w/w), about 90% to about 10% (w/w), about 80% to about 30%, and about 80% to about 40% (w/w), based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

17. The method of claim 15, wherein the concentration of tyloxapol is selected from the group consisting of from about 0.01 to about 90%, from about 1 to about 75%, from about 10 to about 60%, and from about 10 to about 30% by weight, based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

18. The method of claim 15, wherein the effective average particle size of the beclomethasone particles, budesonide particles, or a combination thereof is selected from the group consisting of less than about 120 nm, less than about 100 nm, less than about 80 nm, and less than about 50 nm.

19. The method of claim 15 further comprising adding at least one secondary surface stabilizer to the liquid dispersion medium before or after milling.

20. The method of claim 19, wherein the secondary surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hydroxypropyl methylcellulose, carboxymethylcellulose sodium, methylcellulose,

hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, poloxamers, poloxamines, charged phospholipids, dioctylsulfosuccinate, Tetronic 1508®, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfates, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isobutylphenoxy poly-(glycidol), C₁₈H₃₇CH₂(CON(CH₃)-CH₂(CHOH)₄(CH₂O)₂, decanoyl-N-methylglucamide, n-decyl β-D-glucopyranoside, n-decyl β-D-maltopyranoside, n-dodecyl β-D-glucopyranoside, n-dodecyl β-D-maltoside, heptanoyl-N-methylglucamide, n-heptyl β-D-glucopyranoside, n-heptyl β-D-thioglucoside, n-hexyl β-D-glucopyranoside, nonanoyl-N-methylglucamide, n-nonyl β-D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl-β-D-glucopyranoside, octyl β-D-thioglucopyranoside, and random copolymers of vinyl acetate and vinyl pyrrolidone.

21. The method of claim 19, wherein the secondary surface stabilizer is selected from the group consisting of dioctylsulfosuccinate, sodium lauryl sulfate, hydroxypropylmethyl cellulose, benzalkonium chloride, and polyvinylpyrrolidine.

22. The method of claim 15, wherein the beclomethasone and/or budesonide particles are crystalline, semi-crystalline, amorphous, semi-amorphous, or a mixture thereof.

23. A method of making a nanoparticulate composition comprising:
- (a) dissolving beclomethasone, budesonide, or a combination thereof in a solvent;
 - (b) adding the solubilized beclomethasone, budesonide, or a combination thereof to a solution comprising tyloxapol to form a clear solution;
 - (c) precipitating the solubilized beclomethasone, budesonide, or a combination thereof having tyloxapol adsorbed on the surface thereof using a non-solvent; and

(d) sterile filtering the resulting nanoparticulate dispersion,
wherein the resulting composition of nanoparticulate beclomethasone,
budesonide, or a combination thereof has an effective average particle size of less
than about 150 nm.

24. The method of claim 23, wherein the beclomethasone particles,
budesonide particles, or a combination thereof are present in an amount selected from
the group consisting of about 99% to about 1% (w/w), about 90% to about 10%
(w/w), about 80% to about 30%, and about 80% to about 40% (w/w), based on the
total combined dry weight of beclomethasone, budesonide, and tyloxapol.

25. The method of claim 23, wherein the concentration of tyloxapol is
selected from the group consisting of from about 0.01 to about 90%, from about 1 to
about 75%, from about 10 to about 60%, and from about 10 to about 30% by weight,
based on the total combined dry weight of beclomethasone, budesonide, and
tyloxapol.

26. The method of claim 23, wherein the effective average particle size of
the beclomethasone particles, budesonide particles, or a combination thereof is
selected from the group consisting of less than about 120 nm, less than about 100 nm,
less than about 80 nm, and less than about 50 nm.

27. The method of claim 23 further comprising adding at least one
secondary surface stabilizer to the liquid dispersion medium before or after milling.

28. The method of claim 27, wherein the secondary surface stabilizer is
selected from the group consisting of cetyl pyridinium chloride, gelatin, casein,
phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid,
benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol,
cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers,
polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters,

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polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hydroxypropyl methylcellulose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, poloxamers, poloxamines, charged phospholipids, dioctylsulfosuccinate, Tetronic 1508®, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfates, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isobutylphenoxy poly-(glycidol), C₁₈H₃₇CH₂(CON(CH₃)-CH₂(CHOH)₄(CH₂OH)₂, decanoyl-N-methylglucamide, n-decyl β-D-glucopyranoside, n-decyl β-D-maltopyranoside, n-dodecyl β-D-glucopyranoside, n-dodecyl β-D-maltoside, heptanoyl-N-methylglucamide, n-heptyl-β-D-glucopyranoside, n-heptyl β-D-thioglucofuranoside, n-hexyl β-D-glucopyranoside, nonanoyl-N-methylglucamide, n-nonyl β-D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl-β-D-glucopyranoside, octyl β-D-thioglucopyranoside, and random copolymers of vinyl acetate and vinyl pyrrolidone.

29. The method of claim 27, wherein the secondary surface stabilizer is selected from the group consisting of dioctylsulfosuccinate, sodium lauryl sulfate, hydroxypropylmethyl cellulose, benzalkonium chloride, and polyvinylpyrrolidone.

30. The method of claim 23, wherein the beclomethasone and/or budesonide particles are crystalline, semi-crystalline, amorphous, semi-amorphous, or a mixture thereof.

31. A method of treating a patient in need with a nanoparticulate composition comprising administering to a patient in need a therapeutically effective amount of a nanoparticulate composition of budesonide, beclomethasone, or a combination thereof, wherein said composition comprises:

- (a) budesonide, beclomethasone, or a combination thereof having an effective average particle size of less than about 150 nm; and
 - (b) tyloxapol adsorbed on the surface of the budesonide and/or beclomethasone,
- wherein the nanoparticulate composition has been sterile filtered.

32. The method of claim 31, wherein said treatment is for an inflammatory disease.

33. The method of claim 31, wherein said treatment is for asthma, cystic fibrosis, or chronic obstructive pulmonary disease.

34. The method of claim 31, wherein said composition is administered via a nasal or pulmonary aerosol.